REMARKS

The specification at page 15, line 17 was amended to delete the phrase "orotic acid". The amendment is made to delete this term since it was objected to as new matter by the Examiner. However, Applicant wish to point out to the Examiner that Vitamin B13 is also known as orotic acid to one of ordinary skill in the art. Support for the amendment is found in the originally filed specification.

**RESPONSE**

Claims 1 - 4 were rejected as being obvious in view of Applicant's prior Chinese Patent No. 1129113 (CN 113) in combination with Weischer et al, Shenfield, Pauza et al, Haines et al, and Asanaka et al, both of record and newly cited.

The Examiner's position is that CN 113 described a medicament suitable for the treatment of AIDS wherein the composition comprised methionine, silybin, Vitamin B3, Vitamin C, Vitamin B6, folic acid, and thioctic acid with various pharmaceutical carriers and excipients. Weisher et al. taught the use of Vitamin A, Vitamin B1, Vitamin B6, Vitamin B12, and Vitamin C in combination for the same purpose. Shenfield taught the use of glycerophosphate as a pharmaceutical carrier. Pauza et al taught Vitamin D in combination with carriers and excipients for the treatment of AIDS. Haines et al and Asanaka taught the use of Vitamin B5. These ingredients were taught individually of in combination as being useful for the treatment of AIDS.

To support a rejection for prima facie obviousness, it is necessary to consider the factors set forth in Graham v. John Deere Co., 383 US 1, 17-18. The factors are:

1. Determine the scope and contents of the prior art;
2. Ascertain the differences between the prior art and the claims at issue;
3. Determine the level of skill in the pertinent art; and
4. Evaluate any evidence of seconday considerations.

Thus, it is necessary to review the claimed invention and the cited prior art to determine what is claimed and what are the contents of the cited reference.

Claims 1-4 of the present application are directed to 4 specific formulations for

the treatment of AIDS. Claim 1 represents the broadest in scope and recites a formulation:

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| DL-Methonine | 5-800 |
| Silybin | 25-400 |
| Thioctamide | 10-200 |
| Brompheniramine Maleate | 2-36 |
| Dexamethasone | 0.2-4 |
| Vitamin A | 0.01-0.04 |
| Thiamine | 10-300 |
| Riboflavin | 1-20 |
| Nicotinamide | 5-300 |
| Pyridoxine Hydrochloride | 50-200 |
| Folic acid | 2-20 |
| Cyanocobalamin | 0.02-0.2 |
| Ascorbic Acid | 10-2000 |
| Calcium Glycero Phosphate | 10-500 |
| Pantothenic Acid | 20-100 |
| Vitamin D3 | 0.00001-0.0003. |

The primary reference cited was CN 113. This is Applicant's prior Chinese Patent. It described a medicament for the treatment of AIDS consisting of 13 ingredients by weight as follows:

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| DL methionine | 10-4500 |
| Silybin | 5-150 |
| Thiamine | 5-300 |
| Niacinamide | 5-400 |
| Vitamin C | 20-700 |
| Vitamin B13 | 10-350 |
| Vitamin B6 | 5-150 |
| Folic acid | 2-30 |
| Riboflavin | 2-30 |

| | |
|---|---|
| Dexamethasone | 0/1-2 |
| Bromoprianline maleate | 1-25 |
| Cyanocobalamin | 0.005-0.1 |
| Thioctamide. | 5-150 |

A comparison of the formulation claimed and that described in CN113, the differences in the formulations are:

The formulation of Claim 1 contains the following ingredients not found in CN113 - Vitamin A, Pyridoxine Hydrochloride, Calcium glycerpophosphate Panthothenic acid and Vitamin B5. Whereas, the formulation of Claim 1 does not contain Vitamin B13, or Vitamin B6 found in CN 113. In accordance with the specification of CN 113, all of the ingredients are a part of the medicament effective for the treatment of AIDS. There is no indication that any on of the ingredients can be omitted not any ingredients added. It is to be noted that in particular, one of the major ingredients found in CN113, Vitamin B13 is not found in the formulations as claimed.

Applicant is familiar with the medicament of CN 113 and had used the formulation to treat AIDS patients in Thailand and in China. In many of the cases, the formulation of CN113 was effective. Enclosed herewith is a statement by Shuwen Lee with the English translation. The statement and accompanying information were prepared by Shuwen Lee himself without help from any lawyer. Accompanying the statement is a summary of five specific cases showing that the AIDS patients who were treated with the claimed formulation show improvements in decrease of viral load and CD4 cell count. Whereas, in five other cases treated previously with the formulation of CN 113, four of the patients failed to show improvement and died. A Table comparing the results obtained shows the results in comparison. The statement is also accompanied by the confidentail clinical records of two patients who were treated in Thailand from the period of 1994 to 2001. The dates in the report were translated by Ai-min Lan, a Thai of Chinese origin. The data obtained showed that the formulations claimed are highly effective for the treatment of AIDS and provides an improvement over the formulation of CN113. This is unexpected.

It is believed that the data supports a finding that the claimed invention is not

prima facie obvious over CN113 alone.

Applicant traverses the Examiner's position that Weischer et al taught that a formulation containing Vitamin A, Vitamin B1, Vitamin B6, Vitamin B12 and Vitamin C as being useful for the treatment of AIDS. A detailed reading of Weischer et al. shows that the principal ingredient taught by Wischer et al is alpha lipoic acid. Further, Weischer et al requires the presence of Vitamin E. A combination of Weischer et al would still require the presence of alpha lipoic acid and Vitamin E. Whereas, this principal ingredient and Vitamin E are completely absent from the claimed formulation. There is nothing in Weischer et al to indicate that these ingredients can be omitted. Thus, the claimed invention cannot be regarded as obvious in view of Weischer et al alone or in combination with CN 113.

A review of Shenfield suggests that calcium glycerophosphate is effective for the treatment of HIV infection. Example 16 showed that the doses used were 100 mg/day for two weeks followed by 300 mg/day for the third week. There is no teaching to use calcium glycerophosphate with the other 15 ingredients of the claimed formulation.

Pauza et al taught the use of Vitamin D compounds including Vitamin D3 to inhibit the replication of HIV in human cells. However, a careful review of the test results show that Vitamin D analogs were helpful in the differentiation of human leukemia cells, HL-60. It is not clear how this activity is related to the replication of HIV in human cells. On page 60 of Pauza, there is a statement that α1-hydroxylated Vitamin D compounds is effective to reduce the replication of lentivirus in vitro. Athough HIV is included in the family of lentivirii, it is clear based on the knowledge of those of skill in the art that the reduction of lentivirus replication in vitro cannot be related to the reduction of HIV in living human cells. The deficiency of Pauza et al. was not taken into consideration by the Examiner.

Haines et al., also cited, teaches the use of lidocaine for the treatment of herpes and it also taught that pantothenic acid can be added to lidocaine as an effective antiviral agent against HIV. The claimed formulation does not contain a combination of pantothenic acid with lidocaine. Thus, Haines does not add anything to the teachings of

Asanaka et al. disclosed the testing of lorazepam, calcium hopantenate, prochlorperazine maleate, amantadine HCl, perphenazine and nitrazepam for antiviral activity. Among these, only perphenazine and nitrazepam show antiviral activity without cytoxicity. Of the two, only perphenazine showed weak anti-HIV activity. Thus, according to Asanaka, none of the agents he tested were effective against HIV except for the weak anti-HIV activity of perphenazine. There is no mention of antiviral activity of Vitamin B5, pantothenic acid. In fact, it would appear that Asanaka et al taught against the use of Vitamin B5.

The claimed formulation does not contain perphenazine. Thus, it cannot be said that the claimed invention is obvious in view of Asanaka et al alone or in combination with the other cited references.

In the determination of obviousness, it is the prior art as a whole that has to be taken into consideration. It is not proper to take pieces of the prior art and cobble these pieces together.

It is Applicant believe that the invention as claimed has been show by use in AIDS patients to be effective for the treatment of AIDS. This is in contrast to the disclosure of the cited references where the compounds were only tested in cells of in vitro. Based on the surprising result obtained in actual patients, it is believed that claims 1-4 directed to the formulations that have been tested and used are allowable. An early allowance is requested.

Respectfully submitted,
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